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STAGES AND FORMS OF SYPHILIS,

WITH MORE ESPECIAL REFERENCE TO THE

HEPATIC MANIFESTATIONS OF THE DISEASE.

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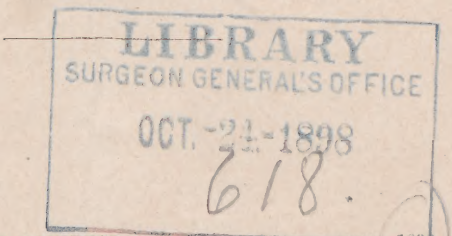

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ON THE STAGES AND FORMS OF SYPHILIS WITH MORE ESPECIAL REFERENCE TO THE HEPATIC MANIFESTATIONS OF THE DISEASE.[1]

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It is remarkable how during all these centuries, syphilis has remained sharply distinguished from all other forms of human disease, constituting a class apart. There are many other contagious maladies, not a few chronic infectious disorders, and, now-a-days, we are able to group these together; we can recognise common principles governing their course and effects upon the organism, and can see, or think we see, a common principle underlying the morbid changes in one or other tissue from the onset of the disease to its culmination—a principle identical in the infant and in the aged. So we can with syphilis —only habitually we do not. We treat and regard it as a something distinct.

Take for instance that disease which in its chronicity as in the lesions which characterise it, most closely resembles syphilis—tuberculosis. From the onset to the end, at every stage, from the primary lesion to the most extensive generalisation of the process, we see one morbid change at work, namely, the focal multiplication of the bacilli leading to the development of tubercles. It is true that according to circumstances these tubercles may vary in their characters from a condition in which small cell infiltration is so extensive as closely to approximate to miliary abscess formation, through conditions of so-called epithelioid cell overgrowth to a state in which fibroid connec-

[1] Delivered at the meeting of the Ontario Medical Association at Toronto, June 1st, 1898.

tive tissue development is so excessive as to mask everything else, save, perhaps, necrosis and caseation. But the fact remains that we do not sharply differentiate successive stages of the disease, or consider that the successive stages are characterised by the development of specific manifestations. At the most, in one organ, the lungs, we trace such successive stages of the tubercular process, but we never think of laying down that what is to be made out in the lungs obtains for other organs, and for the body in general. On the contrary, a study of pulmonary phthisis alone has convinced us that the course of tuberculosis varies so greatly according to the interaction of two factors—the condition or reactive power of the tissues, and the virulence of the bacilli—that to attempt to plot out the course of the disease in each case into well defined stages is an impossibility.

With syphilis it is quite another thing. From Ricord onwards a primary, secondary, and tertiary stage have been clearly distinguished, and not only this, but according as to whether the disease is acquired in post-natal life, or has seized upon the individual while in the mother's womb, so do we recognise two different types of the disease.

There is, I take it, no more firmly 'fixed idea' in the whole of medicine than that of the absolute existence of these different stages and forms of syphilis. To-day, I do not want to pose as a revolutionist and an iconoclast, for speaking broadly, and regarding the bulk of the evidence before us, I, like all others, must acknowledge the utility of the divisions. But there is a danger in these fixed ideas, in medicine as in all sublunary affairs, and, to say the least, it is of benefit occasionally to enquire whether what is accepted of all men is so absolutely and entirely fixed and assured as we are accustomed to regard it.

What I am about to say is not novel. The unity of syphilitic lesions has been preached for now more than thirty years, in fact, ever since Wagner pointed out that all such lesions might be referred to the developments of a specific neoplasm. Perhaps Wagner went too far, for there are generalised fibroid conditions, which, as I shall have to point out in connection with the liver, are not directly due to the development of circumscribed neoplasms; but it must be acknowledged that neoplasms or infective granulomata are to be recognised in each stage and form of the disease. Nevertheless, the idea of the sharp demarcation of the different forms and stages of the disease seems to be as firmly planted to-day as it was prior to 1864, and the admirable protest of Nevins Hyde[1] and the writings of others do not seem as yet to have influenced the profession in general.

[1] Morrow's System of Genito-Urinary Diseases, Vol. II., 1893, p. 20, *et seq.*

At the outset, I must point out that it is not even necessary to have any recognisable first stage or cutaneous chancre. We know well, that in every case of infection, the infectious agent must make an entry from without into the tissues, and in a great number of cases we can discover the point or points of entry, and at such point or points we find evidences of primary local infection, whether on the skin or mucous membranes, and this local infection is strictly comparable with the cutaneous syphilitic chancre. But we also come across cases in which there is a complete lack of evidence of such superficial primary infection; we may find, for instance, the cervical or mesenteric lymph glands affected with tuberculosis without a sign of tuberculosis of the pharynx or tonsils or intestinal mucosa, cases which usually, though mistakenly, are spoken of as 'cryptogenetic.' What occurs in other diseases must at times occur in syphilis, and in going over my post-mortem records, in which to each case, I have subjoined a record of the clinical history of the case, I have been struck several times by observing that where well marked tertiary syphilis has been present in the organs, there has not been a sign of old penile or other chancre,[1] and more than once, in following up the clinical history, by finding that while the patient has freely admitted that he has led a loose life and suffered, it may be several times, from gonorrhœa, he has denied ever having suffered from chancre (vide case III). Now presumably an individual who had had a hard sore would not wholly forget the circumstance, nor is it rational to urge that a hospital patient who admits without constraint that he has led a life of excess and suffered from other venereal diseases, would conceal the previous existence of a chancre. Either then the chancre was so small and inconsiderable as to cause no inconvenience, or the virus gained entry into the system without causing any cutaneous disturbance.

In the female this absence of any superficial or recognisable first stage is especially noticeable; time after time the disease only manifests itself in the secondary stage. I would go so far as to say that the 'fixed idea' that there must be a chancre developed at the region of primary infection, has led to a thorough and general misunderstanding as to the nature of congenital syphilis. It is a popular fallacy to regard a considerable number of cases in which the father of

[1] In some at least of these cases without doubt, the same process has happened as occurs occasionally in connection with vaccinal cicatrices, namely, there has been so complete absorption of the cicatrical tissue, that the part becomes in the course of years absolutely normal in appearance. This complete absorption I need scarcely say, is characteristic of primary lesions of mucous surfaces, and is very frequent in the female.

syphilitic offspring is syphilitic, and the mother is apparently free from the disease, as due to the sperm being syphilised, or if this view be carried to its logical conclusion, it is supposed that the spermatozoon bears with it the syphilitic virus, be it bacillus or whatever the nature of the specific microbe, and introduces it into the ovum at the moment of conception, and thus the offspring develops, syphilised from the start, the mother being and remaining absolutely free from taint. This, as I say, is a popular fallacy. But it is incredible that the germ gain entrance into the spermatozoon, for the spermatozoon being nucleus and flagellum, and scarce anything more, has not the means of ingesting foreign bodies, while we have not a shred of evidence that the syphilitic germ is amœboid and capable of making its way into the spermatozoon.

It is likewise outside the limits of credibility that a virulent organism could be within the minute almost yolkless segmenting human ovum, lying latent in one or other of the cells, the products of segmentation. Such passages of pathogenic microbes on to the surface, and possibly into the eggs, may occur in insects, as Pasteur demonstrated, but the insect's egg contains relatively abundant yolk, and segmentation then may be little influenced by the presence of the micro-organism, provided that this be in the yolk. Even then, I doubt whether the embryo could develop properly, and am inclined to consider that a more reasonable explanation of Pasteur's observations upon the silk worm's eggs is, that at a relatively late period of their development those which come to maturity become tainted either from the surface or from other eggs which have been killed by the multiplication of the germs within them.

If the syphilitic virus gained entry into the unsegmented human ovum, its effects would surely be to lead to the destruction of the ovum. Fœtal syphilis must originate at a later date, and although syphilis in the parents may doubtless have its effects upon the ovum and spermatozoa of the same, and lead to constitutional disturbances in the offspring, progressive syphilitic lesions, the true syphilomata, in the fœtus and infant are *not* inherited, but are congenital, that is to say, acquired in utero after conception. Or in other words, inherited and congenital syphilitic lesions are two very different things. Thus to return to the main point, if the mother be without sign of syphilis, and the child be syphilitic, the only satisfactory explanation is, that the syphilitic virus has entered into the maternal organism and tissues, and has failed to induce any characteristic lesion at the point of entry, but has, nevertheless, through the placenta and chorionic villi gained an entrance into the fœtal tissues ; the process arrested

in the mother has been developed in the susceptible tissues of the child, and we have here an interesting example of the variability in the manifestations of the disease dependent upon the reactive powers of the tissues.

Were any further word necessary in support of this contention it would be found in the significant way in which the liver is affected in congenital syphilis. Extensive specific lesions of the liver in the acquired disease are relatively uncommon. They are the most common of all lesions in the congenital affection. As Chiari has pointed out, out of 144 cases of congenital syphilis examined by him, the liver was diseased (and that extensively) in 123 cases or nearly nine-tenths. Were the ovum infected it would be difficult to explain why the liver should thus be especially singled out. When we remember that this organ is the first to receive the blood coming by the umbilical vein, then if the infection originates from the placenta hepatic implication is the natural sequence.

The essential difference between such congenital, or ante-natal, and 'acquired,' or post-natal syphilis is, that in the former the virus passes immediately into the blood and so becomes disseminated through the organism, in the latter, the dissemination is delayed. The second stage of acquired syphilis, is the first stage of the congenital disease.

Again, although as a pathologist not in practice, I have not met with and am little likely to come across the condition, continuing the analogy between tuberculosis and syphilis[1] we must, I hold, admit the inherent probability of Kaposi's statement that it is possible to have a primary cutaneous syphilitic lesion, a true specific indurated chancre, not followed by any secondary effects. And further it is well established that women who have borne syphilised children and have themselves shown not a sign of primary or secondary manifestations may, years after, present unmistakable tertiary lesions.[2]

Up to this point, therefore, it may be laid down :

(1) That from analogy, as from clinical history and absence of any indications of the same, in sundry cases there may be an absence of the primary cutaneous or epithelial manifestations of syphilis.

(2) That individuals may fail to present either primary or secondary symptoms that are recognisable, and yet eventually develope definite tertiary lesions of the disease.

(3) That where the subject is relatively insusceptible, it is possible

[1] Every pathologist knows, many from personal experience, how frequent among those performing autopsies are cases of strictly localised cutaneous tubercles not followed by extension. Such primary cutaneous tuberculosis is characterised by its tendency to remain localised.

[2] Vide Finger, Arch. f. Dermat. u. Syph. 1890, p. 331.

that the disease may be limited to the primary cutaneous manifestation not followed by secondary lesions..

(4) That as with tuberculosis so with syphilis, the congenital form of the disease begins at what may be termed the secondary stage of the acquired disease, *i.e.*, the stage of general dissemination of the virus through the organism.

The Relationship between Secondary and Tertiary Syphilis.

I would now pass on to consider the relationship between the secondary and tertiary stages of syphilis.

Where in any infectious diseases we have widespread eruptions, affecting both skin and mucous membranes, we now feel assured that such eruptions are due either to the irritation set up by the actual presence and growth of the specific germs of that disease in the subcutaneous and submucous layers, or to the irritation produced by the products of these germs growing in other parts of the system. And the more we study infections of which we can isolate the specific microbes (streptococcus and pyococcus infections, typhoid, &c.), the more we find the first of these alternatives in force, and in the case of syphilitic eruptions, the fact that the cutaneous eruptions are infective, affords clear evidence that the specific virus is present in them.

Such generalised infections of the skin and mucus membranes can only be brought about through the agency of the blood stream, or, otherwise, what is termed the secondary stage of post-natal, acquired syphilis, is the stage of general dissemination of the virus through the system by the blood stream, and of the more immediate results of such dissemination. What has been described as the second period of incubation (the interval elapsing between the development of the chancre and the appearance of syphilodermiæ) is the period requisite for the virus to infect and traverse the lymphatic system on its way from the primary lesion into the blood stream, and then to proliferate in the cutaneous and other tissues up to such a point that eventually it produces a reaction.

It is usually held that the syphilitic virus now especially affects the skin and mucosæ, and that the abundant and varied crop of syphilides—of syphilodermiæ—are the peculiar sign of the second stage gummatous and more fibrous growths being characteristic tertiary developments. Certainly the eruptions are the prominent features of the secondary stage, but it is too much left out of account that in the early stages of generalisation of the disease, the internal organs may be, and perchance often are, affected. And what I wish more especially to bring before you this evening is this lack of sharp definition

between the anatomical changes in early and late generalised syphilis. This lack is well shown by a study of the syphilitic liver ; indeed, it is a study of several cases of syphilitic hepatitis which have been revealed in the post-mortem theatre at the Royal Victoria Hospital during the last four years, which has prompted me to select this more general treatment of the stages and forms of syphilis to bring before you this evening.

The reason why tertiary and secondary syphilis are regarded as so widely distinct is not difficult to comprehend. The disease is rarely directly fatal, especially now-a-days, and it is rarely that we obtain an opportunity to study the viscera during the earlier stages. As Jonathan Hutchinson has pertinently remarked : "The visceral pathology of the secondary stage might form a chapter in the history of syphilis which has not yet been written, and for which we possess few data. It is however, I feel sure, a great mistake to state that there are none to be obtained." In the address from which I take these words, an address which opened a celebrated discussion at the Pathological Society in London in 1876, he pointed out that abundant facts are on record to disprove the assertion that large gummata are not to be seen in the secondary stage. He noted that two cases of death from syphilitic disease of the heart which had come under his notice, had both occurred during the secondary stage and presented myocarditis with gummata, and in one of the two there were also distinct gummata in the spleen and in the testes, while he went so far as to state that the best example of gumma in the liver which he had encountered was in an infant.

To bring forward the evidence presented by the liver as to the identity of the anatomical lesions in the two stages, and as to the continuity or unity of the disease, it will be well to discuss the ways in which the liver is affected in syphilis and run over the different forms of specific hepatic lesions.

It is difficult to realise that scarce fifty years have elapsed since it was first clearly established that the liver is affected in any form of syphilis. The chapter in medical history bearing upon the liver in relation to syphilis is of some interest. Hutten and Fallopius and many of the earliest writers upon the morbus gallicus, held that syphilitic ulcers wherever appearing were the result of a corruption of the humours, the origin of which was to be looked for in the liver which had become diseased from the action of a volatile contagion. Others held that this organ was the first to be affected consecutively to disease of the genital organs. This was when every disease was regarded as due to a disturbance of the humours, and the liver being large and

of unknown functions, the severity of the disease almost naturally led to the liver being seized upon as the guilty party in syphilis. When autopsies became more frequent the implication of the liver became seriously disputed : Paracelsus denied that it had any rôle in disease, stating that he had frequently found other organs affected but had rarely met with any disturbance of the liver. Morgagni again in the middle of the eighteenth century, but expressed the views of his contemporaries when he denied any relationship between syphilis and hepatic disorders.

The Liver of Congenital Syphilis.

Only in 1848,[1] or according to Hutinel and Hudelo in 1847, was there published any serious study of the liver in syphilis, and then it was not the characteristic gummatous liver of the acquired disease, but the enlarged liver of the congenital condition to which attention was called. In that year and yet more fully in 1852, Gubler described the liver of congenital syphilis, pointing out its enlargement, its firmness and elasticity. He noted that the changes were often in circumscribed spots only, and here in these very earliest careful studies upon the subject, he pointed out that while the other lesions in the infant were of a secondary nature, the changes in the liver were of tertiary type and allied to the gummatous developments.

Time forbids that I should describe minutely the histological changes occurring in the liver of congenital syphilis. You will find them clearly stated in an article upon diseases of the liver by your distinguished confrère Dr. Graham, in the recently published Loomis-Thompson System of Medicine, an article which is far and away the best treatise on hepatic disorders by a single individual that has appeared in our language for many years. Suffice it to say that the affected portions of the organ present a combination of the development of minute, somewhat ill-defined collections of small round cells, which we know as miliary gummata, together with a wide-spread development of fibrous tissue, not only along the portal sheaths, but also spreading between the groups of liver cells which present more or less atrophy, in short, a condition of pericellular fibrosis. This fibrosis is in itself what we are accustomed to regard as a peculiarity of tertiary syphilitic manifestations. Yet here it occurs within a very few months of the primary lesion, when cutaneous eruptions and other secondary symptoms are abundant. And not only this, but at times we have appearances more closely resembling the gummata of the acquired disease.

[1] Gubler, Gaz. des Hop. Jan. 1848, and Gaz. Med. de Paris, 1852, p. 262.

What is the meaning of this general interstitial fibrosis, or more correctly, what is the series of changes which leads to its formation ? It is difficult to state with precision. At times it appears to be wholly in excess of any development of the above mentioned miliary gummata. Indeed, it looks as though it had not been preceded by any characteristic syphilomatous lesion, and the peculiar manner in which the connective tissue development extends between the rows of the liver cells, and becomes pericellular, and *pari passu* the liver cells show evidences of atrophy, would seem to indicate that here we are dealing with, not so much the results of the productive granulomatous inflammation, as with a process of tissue disturbance set about by the diffusion throughout the system of the toxic substance generated by the virus. These toxines lead to the atrophy of the liver cells with synchronous development of connective tissue ; in short, the appearances are largely, but by no means entirely, those of a replacement fibrosis.

A somewhat similar condition is occasionally to be met with in the kidney and that in the earlier stages of the disease. The only further point I need impress upon you here is that this generalised fibroid change may be developed in the earliest stage of the generalised disease, and by no means necessarily indicates a tertiary condition.

In some rare cases this extensive fibroid condition appears to be present with very little evidence of syphilomatous or granulomatous change in the organ. Marchand[1] has recently described and collected together about half a dozen examples of this condition. Curiously enough, this form of cirrhotic liver with atrophy in most of the cases has occurred in one of a pair of twins and that one still-born. It is also associated with evidences of profound hepatic disturbance in the shape of icterus. Marchand's cases are not wholly satisfactory so far as regards the history of syphilis in the parents, but, as he states, it is difficult to explain this remarkable condition of atrophy of the organ with extreme fibrosis, save on the supposition that the cases were syphilitic.

Coming now to the presence of gummata, Gubler noted in his earliest communications that scattered through the cirrhotic areas in the infantile liver were numerous fine paler flecks, which he likened to grains of semolina, and Virchow, studying these, spoke of them as miliary gummata. More and more evidence has accumulated as to the relationship between these minute, ill-defined tubercles or collections of small round cells, and the caseous gummata seen in the acquired disease. The relationship is identical with that between

[1] Ctbl. f. Allgem. Path., Vol. VII., 1896, p. 273.

miliary tubercles in the lung, and encapsuled tubercular caseous nodules in the same. In the great majority of cases, the liver of congenital syphilis presents the admixture of a diffuse pericellular cirrhosis and scattered miliary gummata. Sometimes the whole of the organ is affected, at other times the process is observed only in parts, either at the edges or in a portion of one lobe. In this latter case, one has circumscribed yellow masses sharply defined from the, in general, congested, but otherwise unaffected hepatic tissue. Sydney Coupland,[1] indeed, goes so far as to regard these circumscribed masses as enormous gummata. It is, however, open to doubt whether these masses strictly conform to our idea of gummata, although I must confess that it is difficult to define with precision what we include under this term. For myself I am inclined to regard them as more nearly resembling the large nodular syphilomata occasionally to be met with in the adult liver, where they may be so well defined as time and again to lead to the erroneous diagnosis of non-infective neoplasms.

There are frequent cases on record in which true gummata have been recognised in the liver within a few weeks after birth. Several French cases will be found quoted by Hutinel and Hudelo[2] in 1890, while Cohn in 1896 quotes several German authorities.[3] In English literature, I have found cases described by Canton,[4] (in an infant of two weeks, with numerous small gummata), Barlow[5] and Hutchinson (loc. cit.)

In Barlow's case the child showed no syphilitic symptoms until it was seven weeks old; it died five weeks later, and upon the upper surface of the liver were several depressed areas, varying in size from that of a pea to that of an almond, one having a slight tail-like prolongation; there were a few also upon the under surface. As he points out, from these depressions it is clear that the gummata were, as he terms it, *receding*, although it would seem clear that they presented no central caseous change.

From the above description it would seem that in the liver of the new born infant, presenting externally evidence of what is known as as the secondary stage of the disease, there may be several varieties of syphilitic manifestations :

1. Well defined gummata.
2. Admixture of miliary gummata, with generalised fibroid change

[1] Trans. Path. Soc.- London, Vol. XXVII., 1876, p. 303.
[2] Arch. de Med. Experimt, 1890, Vol. II., p. 509.
[3] Virchow's Arch., Vol. 146, 1896, p. 468.
[4] Trans. Path. Soc, Vol. XIII,, 1862, p. 113.
[5] Trans. Path. Soc., Vol. XVII., 1876. p. 292.

not affecting the whole organ but forming relatively large circumscribed areas.

3. Admixture of miliary gummata and generalised fibrosis affecting the whole organ, which is in consequence enlarged.

4. Generalised "atrophic" cirrhosis without much evidence of gummata, but associated with icterus, œdema, etc., the organ being granular and definitely contracted.

In other words all the changes seen in congenital syphilis are those which ordinarily are considered to characterise the tertiary rather than the secondary stage of the disease.

There is yet another form of congenital syphilis which has to be noted; the form termed "Syphilis hereditaria tardiva" or more correctly, delayed congenital syphilis. Several examples of this delayed syphilis are on record; it is to be made out from them that frequently the cutaneous changes may not show themselves for years after birth. Taking up more especially the English literature upon the subject, Henry Morris [1] has described a case of a girl aged 20 with marked syphilitic family history and evidences of interstitial keratitis, who had suffered from sore throat at 12, enlargement of the liver at 18, ascites at 19, and at the autopsy, the liver was found much puckered and deeply fissured as well as altered in shape, while there were several large gummatous nodules imbedded in different parts of the organ. Wills[2] records a case that seems somewhat more definite, in which a male, aged 22, presented a small dense liver with thickened capsule, which was constricted into lobules by numerous thickened bands of connective tissue, a condition which he could only explain as being due to congenital syphilis. Bristowe describes a condition of gummata in the liver of a boy of 15 which gave way to treatment with potassium iodide, a condition which he could only regard as an excellent example of the results of delayed congenital syphilis; and Osler, in his well known Lectures on the Diagnosis of Abdominal Tumours, gives two cases which are similar, one of his own, the other which had been recorded by Dr. A. C. Wood, in the University Medical Magazine, Vol. II. Both of these cases were in boys of 13, presenting clear evidence of congenital syphilis; in both there was the enlarged irregular liver which diminished under the action of potassium iodide. A further case in a male, aged 22, has just been published by Post and Councilman.[3]

It is clear then that congenital syphilis, like the acquired disease, can manifest a tertiary stage long years after infancy, and that the

[1] Trans. Path. Soc. Vol. 21, 1870, p. 214.
[2] Liverpool Medico-Chirurgical Journal, July, 1892.
[3] Boston City Rep., 1898, p. 233.

tertiary symptoms when thus delayed are liable to be of the gummatous type with cicatricial contraction. In other words, congenital syphilis may in every respect follow a course identical with that seen in the acquired.

The Liver of Acquired Syphilis.

Passing on now to consider the syphilitic manifestations in the disease of post-natal acquirement, it is very interesting to notice that whether we are dealing with cases in which death has occurred within the first year after the disease has been communicated to the individual, or whether we obtain the liver long after the acquirement of the disease, the morbid changes are of the same order, the only recognisable difference being that the longer the time that has elapsed after infection, the greater is the tendency to the development of cicatricial changes with contraction and deformity of the organ.

Taking up the hepatic disorders in series, perhaps the earliest disturbance that has been noticed with common frequency is the development of icterus in the early secondary stage. The association has been noticed by several writers. Hilton Fagge, writing in 1867, was able to quote Portal, Ricord, Gubler and Lancereaux upon this point, and noted that Lancereaux alone had collected 21 other descriptions of the connection, and, intermittently, observers have since described the association which is now generally recognised. The last writers upon the subject are Neumann, Joseph, and Uhlmann.

Inasmuch as patients have very rarely died in this stage, it is impossible to state with precision what is the condition, but by analogy with what occurs in the infantile liver, it may be suggested that there is here a generalized toxic disturbance of the organ, with catarrhal hepatitis, which may or may not lead on to the generalised fibroid state which has been described in connection with the infantile liver. Indeed, Hilton Fagge[1] has recorded a very interesting case of what he terms yellow atrophy of the liver consecutive to a diffuse change in the organ due to acquired syphilis. The case is that of a female of 23, in which there was a history of syphilitic rash with falling off of hair, and macular syphilides. Jaundice appeared to be of the obstructive nature. The patient became drowsy, then unconscious and comatose. At the autopsy, the liver weighed 46 oz., and was of an opaque bright yellow colour, and of dense consistence. The surface was mottled, the left lobe resembled very closely that of the infantile syphilitic liver; it was pale and semi-pellucid, and the parenchyma was replaced by connective tissue; there was no amyloid reaction.

[1] Trans. Path. Soc., Vol. XVIII., 1867.

Here then we have the jaundice, associated with the generalised atrophic condition of the organ, which in the absence of full microscopical description, may be taken to be either closely allied to the atrophic form already mentioned in the infant, or to the general pericellular fibrosis with miliary gummata seen in same. Without deciding positively to which form this case belongs, I would point out that generalised change in the organ is more common than I think is generally recognized.

The gummatous syphilitic liver is so characteristic and so well-known a form of hepatic disease, that now-a-days, it is rarely described, save from previous authorities, and thus in general, once gummata are recognized in the liver not much further interest is taken in the case ; thus the old classic descriptions and ideas are perpetuated.

It is generally laid down that in tertiary syphilis affecting the liver, gummata, whether well marked and caseous, or the cicatrised remains of such with well-formed stellate surrounding of fibrous bands are the characteristic changes in the organ, while a condition of generalised and pericellular cirrhosis is wanting. It must, however, be remembered that even years after the primary infection such cirrhotic change may be recognisable, and not a few cases are on record of such a condition.

In three out of eight cases of tertiary syphilis affecting the liver which have come to the post-mortem room at the Royal Victoria Hospital during the past four years, there was clear and fairly extensive pericellular fibrosis along with gummatous change. The fibrosis, it is true, was not generalised over the whole liver, the condition more nearly resembled a condition of circumscribed fibroid change seen in the infantile liver.

These three cases are of some interest as throwing light upon the hepatic changes. In one case there was no clear history given of the date of infection.

Case I.—Male, æt. 35. The patient became anæmic and emaciated in April, 1895, œdema and ascites supervening, and death occurred early in July. There was albuminuria and the œdema of the legs had been complicated with an erysipelatous condition which seems to have been directly caused by the hepatic disturbance, for the heart was fairly normal, and the kidneys although large and white, showed scarce any sign of interstitial change. The liver showed numerous large deep stellate cicatrices with some diaphragmatic adhesions. The organ in general was soft with advanced fatty nutmeg condition. Sections through the cicatrices showed a characteristic gummatous appearance with large bands of fibrous tissue running deeply. Microscopically, there was a considerable amount of pericellular cirrhosis in the neighbourhood of the gummata with much small-celled infiltration. The spleen was large, firm and congested. The stomach presented diffuse submucous hæmorrhages.

I shall return later to consider this condition of small celled infiltration. Case V. to be referred to later showed a similar condition.

In another patient of Dr. Stewart the condition was more widespread.

Case II.—The patient aged about thirty-seven, was infected 14 years before his death, and, although himself a medical man, had never undergone proper antisyphilitic treatment, on account of the intense gastric disturbance induced by mercury and potassium iodide. Four years after infection he suffered from gastritis and diarrhœa alternating with constipation and a condition of gastric disturbance and general malaise which continued at intervals for the rest of his life. It is to be noticed that there was a frequent development of a febrile temperature. Ascites and jaundice supervening in the middle of October he was tapped; the fluid collected again, and he died in the beginning of November.

At the autopsy, there was no sign of old ulceration or chancre; there was well marked jaundice; the heart was healthy in appearance, though there was moderate atheroma of the aorta. There were dense bands of adhesions between the diaphragm and the abdominal wall, and the liver was profoundly contracted and small, scarcely passing beyond the middle line. It had a puckered and coarsely nodular surface. The right lobe was especially contracted presenting frequent and well-marked gummata with surrounding cicatrices so that the surface was broken up into numerous small nodules of the large hobnailed type. On section there were numerous white gummata from two to four mm., in diameter scattered through the liver substance, and in addition there were relatively large areas of fibrosis here and there throughout the organ. The spleen was large, turgid and smooth, weighing 570 grammes.

Upon microscopical examination the organ showed well-formed caseous gummata with a zone of surrounding congestion together with a very general advanced interstitial fibrosis, somewhat irregularly distributed, in addition to the ordinary fibroid bands of tertiary syphilis. The bile capillaries were richly injected with inspissated bile, and the kidney showed a condition of parenchymatous nephritis.

The interest in this is, that here we have presented to us a progressive syphilitic disturbance not arrested to any extent by specific treatment. The amount of change in the liver was extreme, and as above mentioned, consisted in the development of numerous gummata, pericellular fibrosis and catarrhal hepatitis, with jaundice. Indeed, we have here an example of syphilitic infection of the liver in an active stage fourteen years after primary infection. The appearance of the liver in this case appears to throw light upon what is the true nature of so-called tertiary syphilis. This is not by any means a receding process. While the tendency of the disease is, as it were, to burn itself out, and while in the majority of cases, if properly treated, the virus is completely destroyed in the secondary stage, nevertheless there may be persistence of the virus, and under favourable conditions the disease may light up again. Here, in this case, the patient enjoyed very fair health from 1888 to 1893. Gastric and intestinal functions were well performed; he increased in weight, and led an active life. During this time the process was certainly arrested, then the malaise and indigestion returned, and the ascites and jaundice which supervened can only be ascribed to the progressive development of syphilitic disturbance in the liver.

The analogy between syphilis and tuberculosis in this respect is perfect. In about 30 per cent of our autopsies we come upon evidences of old tubercular cicatrices in the lungs, and in the majority of these cases the process is undoubtedly wholly arrested; thus we are dealing with healed tuberculosis. In some however, we see that the virus is still present in the encapsuled caseous masses, for we can in a certain number of cases cause the disease in guinea pigs by inoculating into them the caseous contents of the old tubercles, and again in some cases we can recognise that these tubercles have been obsolescent and not obsolete, for around them we can make out progressive tuberculosis evidently originating from them. Speaking of these cases in the language which we employ to syphilis, we might describe them as being examples of tertiary tuberculosis, or to put it otherwise, we include under the term tertiary syphilis, two conditions:

1. The cicatrices and fibroid changes which are indications of a previous syphilis now healed and obsolete.

2. The lighting up again of an obsolescent syphilis from old foci in which the virus has remained latent.

The two cases just recorded are examples of the latter condition, while the case which follows is one of several examples of the former:

CASE III.—Male, æt. 49, who had led a wandering life in the South American States, Pacific Islands, and over the world since 25. Had suffered from all the diseases of childhood, gonorrhœa at 18, stricture five years later, yellow fever while serving in an American Army, small-pox and malaria when he was 19, had chronic dysentery about six years ago, was a heavy drinker of spirits, and had been a soldier, a sailor, and of late a backwoodsman; he denied having had a chancre. The cause of death was acute lobar pneumonia of the upper lobe of the right lung with purulent peritonitis.

The liver was deformed, weighed 1960 grammes, and showed four large areas of puckering on the upper aspect of the right lobe. A rounded mass 3 cm., broad and 2.5 cm. long projected from the lower end of the right lobe, the truncated end of which was characteristically puckered; the appearance of the organ was typically syphilitic. The intestines showed no signs of previous dysentery.

In this case, the section through the puckerings showed singularly little fibrous tissue despite the extreme contraction and deformity of the region where they were present. There were no proper gummatous areas to be made out, and the only satisfactory explanation is that in this liver which presented so obviously the appearance of tertiary syphilis there had been complete or almost complete absorption of the syphilitic deposits.

It may be suggested that the resemblance between tuberculosis and syphilis which I have thus emphasised is imperfect, in that when tuberculosis once affects the organ, the virus always remains latent in that organ, and there is not the complete absorption which we must acknowledge takes place in the majority of cases in syphilis. For

it is admitted that at the most (and that in untreated cases) only 30 per cent. of those infected show tertiary symptoms. Among those treated the percentage is only about 10 per cent. But this is another modern popular fallacy : there may be complete cure of tuberculosis and complete disappearance of the tubercles even when they have become distinctly fibrous. This is proved by the experimental infection of dogs with peritoneal tuberculosis and arrest of the process by repeated laparotomy. I need scarce remind you that it also has been recognised in some cases that there may be arrest of tubercular peritonitis in man by similar means. Definite cases are on record in which there has been a complete disappearance of well marked fibroid tubercles from the serous coats of the intestines. The analogy, therefore, between tuberculosis and syphilis must be regarded as complete in this respect.

Rarely we come across a syphilitic liver showing very clear evidence of the progressive development of the hepatic condition.

Case IV.—Such a case have I met with in a male of 28, who entered the Royal Victoria Hospital under Dr. Stewart with a rupture of one or more branches of the middle cerebral artery, and who had two years before been treated by Dr. James Bell for syphilis. Whether the syphilis then was primary, secondary, or of later manifestations I cannot ascertain, for the patient died before his history could be elicited. In this case there was syphilitic inflammation of the ventricles of the brain, and early atheroma of smaller arteries. The liver showed three or four puckered scars, and microscopically, fairly frequent gummata, with giant cells and small localised infiltrations of leucocytes. There were no signs of tuberculosis anywhere, and the sections of the liver stained with carbol-fuchsin did not show any tubercle bacilli. In this case, the puckered scars indicated gummata which had undergone cicatrisation and fairly complete absorption. The small infiltration of leucocytes can only be regarded as miliary gummata resembling in every respect those seen in the infantile liver of congenital syphilis. The case must be regarded as one in which, as shown in the ventricle of the brain and in the liver, the active syphilitic process had been rekindled or had progressed with rapidly fatal results.

Case I. was probably an example of the same condition.

The only manifestation of syphilis in connection with the liver which is to be found in the acquired and not in the congenital form, is the condition of perihepatitis. I have not come across or met with in literature any indications of the development or presence of such a condition in the newly born child ; in the adult, more especially at the late stages, it is not very uncommon.

Out of the eight cases, I came upon it in a fairly extensive condition in a female of 62, in which syphilis must have dated back for 20 years, more or less, for she gave a history of having seven children, of which five were miscarriages, and the other two died in infancy. Here the most extensive syphilitic changes were in the neighbourhood of the longitudinal fissure and round the gall-bladder. An interesting point was the fact that a mistaken diagnosis was made of atrophic

cirrhosis with ascites. The capsule of the organ was throughout thickened, the upper surface very smooth, the abnormal lobulation and puckering. Near to the gall-bladder in the right lobe was a caseous nodule, the size of a filbert, showing some calcification on section.

Upon section, the organ showed a thickened fibroid capsule, many small central scars, caseous gummata, and more or less diffuse and apparently recent fibroid change. Here it should be added that during the last five months of her life, she had been repeatedly tapped, and following upon tapping, there was found at the autopsy a condition of sub-acute peritonitis with inflammatory lymph covering the intestines. Thus the perihepatitis might not have been entirely syphilitic indeed I am a little doubtful whether syphilis pure and simple will lead to the condition of generalised perihepatitis.

Case V.—Female, æt. 62, with a history of having had seven children, of which five were miscarriages and the other two died in infancy. The husband said to be phthisical. In 1895, Dr. Roddick removed an epithelial wart, which on examination was found to be non-malignant. Suddenly upon July 31st, 1895, while the patient was feeling in good health she had an attack of hæmatemesis which was repeated next day and again two days later. It was accompanied by melæna and great weakness.

Upon admission to the hospital in August, 1895, under Dr. Stewart, the patient was sallow and there were dilated venules on the face. The liver extended from the fifth rib, two and a half inches downwards; it was not palpable nor could the spleen be felt; there was a low systolic murmur. The urine was high coloured with a trace of albumin. While in hospital epistaxis occurred once or twice. This history together with the progressive loss of flesh, the sub-icteroid tinge, the abdominal swelling with epigastric pain, the slight œdema of the legs, led to a diagnosis of atropic cirrhosis of the liver; 270 ozs. of fluid were removed from the abdomen, and after removal the fulness in the epigastrium was found to be due to the hard large mass passing down to within 8 cm. of the navel. This mass, hard and rounded, was continuous with the right lobe of the liver. The fluid re-accumulated and the patient underwent numerous tappings. She became progressively weaker, and the hepatic tumour appeared to be undergoing progressive diminution.

After having left the hospital she was re-admitted early in January 1896, dying upon January 24th. The condition was thought to be one of atrophic cirrhosis with enlargement of the left lobe.

Autopsy.—Œdema of the legs; extensive ascites with distended abdomen. Upon opening, the visible intestines were found coated with lymph; the omentum which was fatty and œdematous was adherent to the parietes in several places. The liver presented numerous adhesions, especially to the intestines and surrounding organs, specially in the region of gall-bladder. The right lobe did not reach the costal margin, the left extended just below the xyphoid. The organ weighed 1425 grammes, its greatest breadth was 22 cm., the right lobe especially being contracted (breadth 10 cm.); this lobe was also diminished from above downwards, its length being 15.5 as compared with 19 cm., of the left lobe. The capsule was thickened; the upper surface fairly smooth with, however, linear indentations, but the under surface presented extensive abnormal lobules especially in the region of the gall-bladder and upon the right lobe, so that several small lobules of liver tissue were produced, and near to the gall-bladder a caseous nodule the size of a filbert showed some calcification upon section. The under surface of the left lobe showed numerous cicatrices, some distinctly stellate. The largest was close to the longitudinal fissure and was 3 cm. in diameter.

Upon section the organ showed many small central scars, caseous gummata and *more or less diffuse and apparently recent fibroid change*. There was further a moderate amount of chronic passive congestion and cholelithiasis with obstruction of the cystic duct. The organ gave no amyloid reaction, and the spleen was large, firm and tense, with thickened capsule. In addition there was fat necrosis of the pancreas, brown atrophy of the heart, moderate atheroma of the aorta, slight chronic pachymeningitis, emphysema and bronchitis.

It will be noticed that the most extensive syphilitic change was in the neighbourhood of the longitudinal fissure and round the gall-bladder.

Yet another case of syphilitic liver with great thickening of the capsule showed this same complication of peritonitis. In this case (a patient under Dr. James Bell) there had been recurrent attacks of appendicitis during the last four years, with much chronic fibroid typhlitis, and the patient died of acute peritonitis following operation. Although the liver showed numerous stellate scars with abnormal lobulation, these were on the upper surface and there had been no signs of hepatic disturbance. There were in addition moderate arterio-sclerosis and fibroid syphilis of the left testicle.

Case VI.—The patient, a male, entered for recurrent appendicitis and died of acute peritonitis following the operation Feb. 27th, 1896. Four years previously had had illness with symptoms of appendicitis. For five or six weeks before admission had dyspepsia, followed by right iliac pain beginning about Feb. 7th, kept at work till the 12th. Operation: Purulent appendicitis with perforation, followed by general peritonitis and death.

Autopsy.—Acute peritonitis with evidence of much chronic fibroid typhlitis. Liver large, surface very irregular, owing to great irregular thickening of capsule. Weight 2000 grams, numerous large superficial stellate scars with abnormal lobulation; greatest thickening about longitudinal ligament in front. On section, fairly firm, a few small internal cicatrices; portal vein and vena cava free; periportal glands free. Liver showed large periportal fibrous glands with thickened arteries and atrophy of some liver cells. Spleen, large 155 grams, 12.5 x 6.5 x 3 firm, soft and rather pale. Pancreas, hæmorrhages and necrosis. Other organs showed evidences of the acute febrile disturbance with moderate arterio-sclerosis and its effects; there was in addition fibroid syphilis of the left testis.

In the case of a male, æt. 75, the organ had the characteristically puckered appearance and showed upon the anterior surface of the right lobe a large convex cartilaginous plate, 9.5 x 7.5 cm., or about 4 x 5 inches, associated with chronic thickening of the capsule, together with numerous small cartilaginous plates elsewhere; the left lobe did not show much thickening of its capsule. The spleen, however, as is the rule in chronic perihepatitis, presented a much thickened capsule. (In this case there was very extensive gummatous hepatitis with practically no clinical evidence of affection of the organ.)

Case VII.—Of this patient, a male, æt. 76, under Dr. Jas. Bell, with cancer of the tongue and general arterio-sclerosis, there is no history bearing upon the date of infection.

Autopsy.—Emaciation; rheumatoid arthritis of fingers; slight icterus; retracted abdomen, abdominal cavity dry; liver 1335 grams, 21 x 16 x 8 cm, right lobe anteriorly and inferiorly broken up into several small lobules; at hilus five or six small accessory lobules between a bean and a walnut in size. On anterior surface of right lobe,

left superior angle, large convex cartilaginous plate 9½ by 7½ cm. associated with chronic thickening of capsule. Numerous small cartilaginous plates elsewhere on the right lobe, the left also broken up into several lobules. On section, organ fairly friable with here and there small fibrous strands of tissue intersecting collections of lobules. Spleen, capsule very much thickened, weight 240, enlarged 10.5 c 7.5 x 5 cm. On section, soft, with slight fibrosis. Other conditions: Cancer of tongue, arterio-sclerosis, sclerosed heart valves and coronary arteries, hypertrophy of pros: tate, hydronephrosis, chronic interstitial nephritis, etc. (This case again shows very extensive gummatous hepatitis with singularly little clinical evidence of the liver disease.)

In two other cases, there were localised adhesions between the organ and the diaphragm. These adhesions, however, bore no clear relationship to the areas of cicatrisation in the organ.

On the whole therefore I am inclined to regard diffuse chronic perihepatitis as more a complication, than a direct syphilitic manifestation.

There is one further condition of syphilitic disturbance of the liver in the adult to which I have only referred in passing, and that is the development of large tumour-like outgrowths of the organ which are so sharply defined that clinically the erroneous diagnosis may easily be made of malignant neoplasm. These growths are distinct from the bosses produced by the cicatrices of old gummata and subsequent deformity of the organ, and under the action of potassium iodide, they appear to undergo fairly rapid absoption. Osler in the work already cited has described very clearly one of these cases. So far as I know, in the coarse lesion produced, there is nothing quite similar to this seen in congenital syphilis. Microscopically however, the mass shows a condition not unlike that seen in the circumscribed areas of fibrosis in the infantile liver. There may or may not be caseous or gummatous change in the centre. There is however, much central fibroid change with complete destruction of hepatic parenchyma, and towards the periphery there is a more vascular connective tissue area in which strands of liver cells are to be made out. The nature of the growth and the presence of these liver cells would appear to indicate that what we have to deal with in such cases is a focal syphilomatous change in which, as the process extends from the centre, there is, at the same time, a constant proliferation of the liver tissue, and thus gradually, there is the development of a localised mass of new tissue, in the main fibroid, but at the periphery, where the change is not so extreme, there is growing liver tissue.

With this I have, I believe, mentioned the main manifestations of syphilis as they occur in the infant and in the adult, and it will be seen:

In the first place that the lesions occurring in the congenital and

the acquired disease, are identical, and brought about by the same process or processes.

That whether we have to deal with the disease in the secondary or in the tertiary stage, the same processes are at work. That, if we except those cases as truly tertiary in which we have to deal merely with the fibroid remains of obsolete gummata, and again those cases in which there is perihepatitis (which perihepatitis appears to be a complication rather than the genuine and direct result of syphilis), then we are bound to admit that the study of the liver alone would indicate that no sharp boundary line can be made out between secondary and tertiary syphilis. No more can we make out such a boundary between secondary and tertiary tuberculosis.

While I and all others must admit the utility of recognising these two stages, from an anatomical and histological standpoint one is forced to acknowledge that progressive syphilis is characterised by the same succession of phenomena whether it be studied but a few months or long years after the primary infection. Anatomically and histologically there is no valid distinction to be drawn between secondary and tertiary syphilis.

It may be asked whether such a conclusion is not wholly at variance with clinical opinion and experience? Upon the face of it, it is —but if the subject be looked into carefully, I think that such a view will reconcile not a few of the divergencies existing among syphilologists. We have those (and they are the majority) who state that tertiary syphilis is non-infectious, and those who bring forward clear examples of the production of infection five or ten years after primary inoculation of the disease. This difference can be reconciled if we agree upon the following points:

1. That now-a-days, under proper treatment, syphilis, if not a self-limiting disease, is at least a disease which can be healed, so that many of the lesions recognised as being tertiary syphilis, are truly the indications of the old healed syphilis, and not signs of progressive or latent disease.

2, If the disease has not completely died out and remains latent, the resistance of the tissues of the organism is such that in the majority of cases if it does not tend to light up again; there is so considerable a local reaction, that the infection and consequently the spread of the process tend to remain strictly localised, and the germs (which are probably of bacillary nature) do not become disseminated through the blood. Thus neither the blood nor the secretions contain the virus.

3. In a very small number of cases, the reaction on the part of the

tissues may be so lessened, and the virus retain or gain so high a virulence that either it causes ulceration, or in other ways becomes disseminated and capable of causing infection even late in the tertiary stage.[1]

[1] After reading this paper, Dr. C. A. Temple of Toronto, brought to my notice an interesting example illustrating this point which he very kindly permits me to note here. The patient, a vigorous blonde, contracted the initial lesion five years before marriage, underwent mercurial treatment for four years, and later was treated by Fournier's intermittent method, generally for from six to eight weeks twice a year. His wife a highly educated and cultured woman never showed any symptom of syphilis. In the fifth year of marriage she became pregnant for the first time, and, ten years after the primary infection of the husband, she aborted at the seventh month, the fœtus showing the typical facial characteristics and a greatly enlarged liver. The husband had always tended to have syphilitic eruptions if he neglected treatment, and when last Dr. Temple saw him, after the abortion, there were scaling circinate lesions on the abdomen and groins and ulcerating patches, some ecthymatous, others healing, on both legs from the knee downwards.